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溶瘤腺病毒肿瘤靶向治疗：从实验室到临床

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摘要：

过去几十年从实验室到临床对溶瘤腺病毒进行了广泛的研究。有多种策略增强溶瘤腺病毒的肿瘤靶向性，包括将腺病毒基因组中
（如E1A或E1B）进行突变或（和）利用肿瘤特异性启动子调控E1A基因的靶向转录调控，利用不同血清型腺病毒或RGD基序改变溶
转导调控，以及利用细胞载体将溶瘤腺病毒传送至远处的肿瘤部位。溶瘤腺病毒作为一种载体，输送免疫调节基因或治疗性基因，通
胞凋亡、自杀等产生协同抗肿瘤效应。溶瘤腺病毒临床试验涉及到多种实体瘤，显示其临床应用是安全的，毒性作用轻至中度，患者
反应的临床病例较少见，联合诸如化、放疗等治疗方法有助于提高临床效果。未来的方向应强化溶瘤腺病毒免疫学相关机制的研究、
术性瓶颈、优化细胞载体、提高溶瘤腺病毒远处传递的靶向性，以及寻找更具潜能的肿瘤干细胞作为靶点。此外，需要扩大临床试验
特别是免疫治疗联合应用的研究。

关键词：肿瘤 溶瘤病毒 溶瘤腺病毒 靶向治疗

Oncolytic adenoviruses for targeted cancer therapy: From the laboratory to the clinic

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Abstract:

Extensive investigations of oncolytic adenoviruse (OA) from the laboratory to the clinic have been made in
a few strategies for improving the potential targeted therapy of OA in cancer, including transcriptional targetin
genes (such as E1A or E1B) of Ad genome which is involved in the control of cell cycle checkpoints in cells and/
promoter control of E1A expression, transductional targeting by changing tropism of OA with different types or
into tumor cells, and cell carriers for delivery of OA to the distant tumor sites. Enhanced anti-tumor immune res
of tumor cells elicited by OA, as vector, enabling express immunoregulatory or therapeutic genes contribute to
antitumor effects with OA. Clinical trials of OA for various solid tumors have been carried out, in which the appli
presenting well tolerated, mild to moderate adverse events, though few objective tumor responses to patient
Combination of OA with other therapies, such as chemotherapy or radiotherapy can improve clinical efficacy. Fu
development should be focus on strengthening the research on OA-associated immunological mechanisms, bre
bottlenecks hampering deep studies of OA, optimizing cell carries for targeting of OA to distant tumor sites, an
targets such cancer stem cells. In addition, enlarging the range of clinical OA trials and reinforcing the investig
other therapeutic approaches, particularly with immunotherapy, are needed.

Keywords:tumor oncolytic virus oncolytic adenovirus targeted therapy

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